## REMARKS/ARGUMENTS

This responds to the issues raised in the Final Rejection of October 28, 2008 and accompanies a Request for Continued Examination.

Discussion of Amendments to the Claims

Claims 10-12 have been deleted to overcome the rejection under 35 USC § 112, first paragraph.

Discussion of Priority

A certified copy of the Italian priority application was filed in the US PTO on October 15, 2008, nearly 2 weeks before the mailing date of the current action. On October 15, 2008 the undersigned left a telephone message with Examiner Zarek advising him of this filing. According to PAIR the certified copy is listed in the Bibliographic Data as of October 15, 2008 (copy attached). Acknowledgment of receipt of the certified copy is requested. Applicants are entitled to the benefit of November 6, 2002.

Response to the Rejection of Claims 4-9 Under 35 USC §103, First Paragraph

The purpose of Heredia et al., is to show that resveratrol (RV) synergistically enhances the anti-HIV-1 activity of the nucleoside analogues zidovudine (AZT), zalcitabine (ddC), and didanosine (ddI) (*see* the Abstract). In PHA-stimulated peripheral blood mononuclear cells infected with the T-cell tropic isolate HTLV-IIIB, resveratrol alone, at concentrations of 5 μM and 10 μM, had little effect on HIV-1 replication reducing virus production by approximately 10% to 30 % (*see* page 248, column 1, last paragraph). RV resulted in an in vitro significant suppression of viral replication only when combined with ddI, AZT and ddC, potentiating their inhibitory activity (*see* page 249, Fig.1).

Patzold et al., describe the suppression of human immunodeficiency virus-1 (HIV-1) reactivation in latently infected cells by novel indolocarbazole protein kinase C inhibitors (Abstract). The course of the HIV-1 infection is characterized by a short peak of viremia followed by a long and variable period of latent or persistent infection with no symptoms of disease. When the latent HIV-1 is reactivated there is a shift to productive infection that characterizes full-blown AIDS. Transcriptional activation of HIV-1 from latently infected U1 cells is mediated by PKC, in fact virus expression depends on the activation state of the host cell and probably involves the activation of cellular PKC, since stimulation of latently infected cells

with PMA, a known activator of PKC, induces virus replication in a concentration-dependent manner (*see* page 274, II paragraph). Therefore, Patzold et al. teach that indocarbazoles (PKC inhibitors) may lead to the development of antiviral drugs with the potential to inhibit provirus reactivation in early infection (*see* page 274, III paragraph) and preserve the state of latency.

The present invention discloses a method of inhibiting influenza virus replication administering resveratrol, through the inhibition of PKC, a cell enzyme which plays a major role in the influenza virus replication process.

The two documents discussed above refer to HIV-1 which belongs to the Family Retroviridae, Genus Lentivirus, while the present invention refers to the Genus influenza virus, which belongs to the Family Orthomyxoviridae.

Although these two viruses are both RNA viruses, they are very different. In fact, HIV-1 virus is a retrovirus whose RNA genome is retrotranscribed to DNA and integrated in cellular DNA, while the influenza genome is a negative strand RNA not retrotranscribed to DNA. Therefore, the skilled person wouldn't see any analogy between HIV-1 virus and influenza virus. The skilled person would think that these two viruses are not regulated by the same factors and in the same way. As a matter of fact, nobody has ever found a molecule which is able to treat / prevent the infections caused by these viruses. More simply, nobody has ever found an antiviral drug, which is able to treat or prevent all kinds of viral infections. If this was true HIV infections could be treated with anti-influenza drugs and humanity would not suffer from AIDS!

Therefore, the only document that should be considered pertinent to the present invention is Kurokawa et al. that disclose that the growth of influenza virus A/PR/8/34 in MDCK cells is inhibited by H7, a potent inhibitory of protein kinase C (Abstract).

Kurokawa et al. also explain that it is uncertain whether or not the reduction of PKC activity in H7-treated cells is significant for the inhibition of viral growth in MDCK cells. Kurokawa et al., reported that there is no significant difference in protein kinase C activity extracted from H7- and non-H7-treated murine thymoma or T cell hybridoma cell lines. Therefore, the inhibitory effect of H7 on viral growth may be related to some unknown action of H7, rather than to protein kinase C inhibition by H7 (*see* page 2153-4, linking paragraph).

Consequently, since Kurokawa et al. is not clear about the linkage between the reduction of PKC activity and the inhibition of viral growth, one of ordinary skill in the art wouldn't have

substituted resveratrol, a known PKC inhibitor, for H7 since the result of the substitution wouldn't have been predictable.

There was no suggestion or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

Therefore, since the substitution of H7 with another PKC inhibitor had no reasonable expectation of success, the ordinary skill in the art would at most have chosen to substitute H7 with a compound chemically similar to it.

However, the chemical structure of resveratrol (trans-3,5,4'-trihydroxystilbene) is different from the H7 (1-(5-isoquinolinesulphonyl)-2-methylpiperazine dihydrochloride) structure, therefore there is no suggestion from the prior art to use resveratrol instead of H7 and the ordinary skill in the art wouldn't be motivated to use resveratrol instead of H7 because there was no reasonable expectation of success.

Therefore, it was not obvious to try to use resveratrol to inhibit influenza virus replication, because there was no suggestion in prior art to use it and the ordinary skill in the art should have chosen from a infinite number of unidentified and unpredictable solutions with no reasonable expectations of success and undergoing an undue burden of experimentation.

Reconsideration and favorable action are solicited.

Respectfully submitted,

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| 10/533,942 | Use of resveratrol for the preparation of a medicament useful for the treatment of influenza virus infections | 01-27-2009::15:04:01 |
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